IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of	Confirmation No. 3062
HEYDEN et al.	Atty. Ref.: 4662-2
Appln. No. 10/525,959	T.C. / Art Unit: 1654
Filed: February 28, 2005	Examiner: M.A. Audet

FOR: NUTRITIONAL AND THERAPEUTIC COMPOSITION OF AN INSULIN SENSITIZER AND A PEPTIDE FRACTION

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BRIEF FOR EX PARTE APPEAL

March 5, 2008

Mail Stop Appeal Brief – Patents
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Appellants submit this Brief under 37 CFR § 41.37 to appeal the Examiner's final rejections of claims 1, 3, 5, 7-9, 11-12 and 19-21 as set forth in his Office Action mailed May 4, 2007. The fee required under 37 CFR § 41.20(b)(2) is attached.

The Notice of Appeal was timely filed on November 5, 2007. Therefore, this Brief was initially due on January 5, 2008 and is extended by two months by the attached petition and fee required under 37 CFR § 1.136.

Reversal of the Examiner's claim rejections by the Board of Patent Appeals and Interferences (the "Board") is respectfully requested.

I. REAL PARTY IN INTEREST

The assignee DSM IP Assets B.V. holds all rights in the subject invention by the assignment recorded in the U.S. Patent and Trademark Office on February 28, 2005 starting at reel 016985 and frame 0874.

II. RELATED APPEALS AND INTERFERENCES

Appellants, the assignee, and its legal representative do not know of any prior or pending appeal, interference, or judicial proceeding which is related to, directly affects or is directly affected by, or has a bearing on the Board's decision in this appeal.

III. STATUS OF CLAIMS

Claims 1, 3, 5, 7-9, 11-12, 14-21 and 23-26 are pending. Claims 1, 3, 5, 7-9, 11-12 and 19-21 stand rejected and are at issue in this appeal. Claims 14-18 and 23-26 were withdrawn from consideration. Claims 2, 4, 6, 10, 13 and 22 were canceled without prejudice or disclaimer. The claims at issue in this appeal are set forth in the Claims Appendix.

IV. STATUS OF AMENDMENTS

An Amendment was submitted under 37 CFR § 1.116 on August 6, 2007. The Examiner stated in his Advisory Action mailed November 6, 2007 that the amendment would be entered.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The invention involved in this appeal is directed to a composition suitable for oral consumption comprising an insulin sensitizer and a peptide fraction of a protein hydrolysate. At least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da; at least 20 molar% of peptides with a molecular weight below 2000Da are present as di- and/or tripeptides. These limitations are required by pending independent claim 1, which is a combination of original claims 1, 6 and 13. Support can at least be found in the specification at page 6, lines 3-4; page 6, lines 13-15; page 8, lines 19-20; and page 8, lines 22 and 23-24. Therefore, the only independent claim at issue in this appeal is clearly supported by Appellants' disclosure as originally filed.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

A. Under 35 U.S.C. 103(a), was it proper to reject claims 1, 3, 5, 7-9, 11-12 and 19-21 as allegedly unpatentable over Sung (EP 1172373) in view of van Loon et al. (US 6,713,082)?

B. Under 35 U.S.C. 112, 2nd paragraph, was it proper to reject claims 1, 3, 5, 7-9, 11-12 and 19-21 as allegedly indefinite?

VII. ARGUMENTS

The claims stand or fall together.

35 U.S.C. 103 – Nonobviousness

To establish a case of *prima facie* obviousness, all of the claim limitations must be taught or suggested by the prior art. See M.P.E.P. § 2143.03. A claimed invention is unpatentable if the differences between it and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art. *In re Kahn*, 78 USPQ2d 1329, 1334 (Fed. Cir. 2006) citing the legal standard provided in *Graham v. John Deere*, 148 USPQ 459 (1966). The *Graham* analysis needs to be made explicitly. *KSR v. Teleflex*, 82 USPQ2d 1385, 1396 (2007). It requires findings of fact and a rational basis for combining the prior art disclosures to produce the claimed invention. See *id*. ("Often, it will be necessary for a court to look to interrelated teachings of multiple patents . . . and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue"). The use of hindsight reasoning is impermissible. See *id*. at 1397 ("A factfinder should be aware, of course, of the distortion caused by hindsight bias and must be cautious of arguments reliant upon *ex post* reasoning"). Thus, a rejection under Section 103(a) requires "some rationale, articulation, or reasoned basis to explain why the conclusion of [*prima facie*] obviousness is correct." *Kahn*, 78 USPQ2d at 1335; see *KSR*, 82 USPQ2d at 1396. An inquiry should be made as to "whether the improvement is more than the predictable use of prior art elements

according to their established functions." *Id*. at 1396. But a claim which is directed to a combination of prior art elements "is not proved obvious merely by demonstrating that each of its elements was, independently, known in the prior art." *Id*. at 1396. Finally, a determination of *prima facie* obviousness requires a reasonable expectation of success. See *In re Rinehart*, 189 USPQ 143, 148 (C.C.P.A. 1976).

A. Claims 1, 3, 5, 7-9, 11-12 and 19-21 were rejected under Section 103(a) as allegedly being unpatentable over Sung (EP 1172373; hereinafter "Sung") in view of van Loon et al. (US 6,713,082; hereinafter "van Loon"). Appellants traverse.

Sung relates to use of a zinc oligopeptide of six amino acids and having a MW of 800 to 1200 daltons. It does not disclose di- and/or tripeptides in its composition. The zinc is involved in the onset of diabetes mellitus; it is described to have a physiological activity associated with sugar control and vigor in the body (see [0003] of Sung). The peptide is absorbed by the body, see [0012] and [0016]. Thus, the combination of zinc and oligopeptide is intended to increase absorption of Sung's composition by the human body. The function of the peptide is nothing else than to enhance absorption zinc by the body. Sung does not teach or suggest any other use of the oligopeptide. Therefore, the primary document relates only to the use of an oligopeptide of six amino acids to increase the absorption of the zinc by the human body. No shorter oligopeptide (i.e., a dipeptide or tripeptide) is taught or suggested.

In contrast, Appellants' claimed invention requires the presence of (i) an insulin sensitizer and (ii) a large amount (i.e., at least 70 molar%) of peptides having a MW below 2000 daltons with a significant portion (i.e., at least 20 molar%) of peptides being di- and/or tripeptides. It is the presence of a significant proportion of such small peptides (and the optional free amino acids) that are responsible for the efficacy of the claimed composition. Here, potentiation of the insulin sensitizer's activity by small peptides (e.g., di- and/or tripeptides) is not taught or suggested by the prior art. Moreover, no reason is provided by the Examiner for including such small peptides in the composition (i.e., much shorter than Sung's oligopeptide of six amino acids).

Furthermore, no insulin sensitizer is taught or suggested by Sung. And there is no teaching or suggestion in the cited document that other oligopeptides are included in

the composition (i.e., peptides smaller than six amino acids long), nor that the oligopeptides have any effect in diabetes patients to sensitize them to insulin. The Examiner failed to make an inquiry into "whether the improvement is more than the predictable use of prior art elements according to their established functions" as required by the Supreme Court. *KSR*, 82 USPQ2d at 1396. Further, he failed to provide any reason for one of ordinary skill in the art to reduce the length of Sung's oligopeptide.

van Loon relates to hydrolysates combined with the two free amino acids leucine and phenylalanine to enhance the blood insulin level in a healthy person after physical exercise (see van Loon's abstract and claim 24). Col. 1, lines 38-50, explains that this composition consisting of hydrolysate and two specified free amino acids is used to stimulate the plasma insulin response, the synthesis of muscle glycogen, and recovery when taken after exercise. van Loon has nothing to do with diabetes patients, nor does the cited document teach or suggest an insulin sensitizer in combination with small peptides (e.g., di- and/or tripeptides). The specific proportions of small peptides required by Appellants' claimed invention are neither taught nor suggested. In the three examples, van Loon tests a group of healthy male subjects (study 1), male athletes (study 2), and male athletes (study 3). The subjects were not diabetic patients who would be treated with an insulin sensitizer. Thus, there would be no reason to include an insulin sensitizer in van Loon's composition.

Even if the cited documents are combined as proposed by the Examiner, they lack any teaching or suggestion of an insulin sensitizer combined a peptide fraction of a protein hydrolysate containing <u>small</u> peptides (i.e., di- and/or tripeptides). Note that free amino acids are <u>not</u> peptides. The difference between a free amino acid and a peptide is well known to persons skilled in the art and this distinction is also cited in the definitions provided on page 8, lines 14-15, of Appellants' specification. Further, it is improper for limitations of Appellants' claims to be disregarded when comparing their invention and the prior art (see the Examiner's assertion on page 4 of the Action, "Whether . . . any of these references actually expressly teach 70 molar% of these amino acid/peptide fractions to be under 2000 Da is presently deemed immaterial to . . . this invention"). Regardless of whether the Examiner deems them immaterial, Appellants' claims are

directed to a composition comprising (i) an insulin sensitizer and (ii) specific molar% of small peptides. In accordance with *Graham*, in an obviousness rejection, the Examiner is required to determine whether or not the claim limitations are disclosed in the cited documents because such is a prerequisite for determining the differences between the claimed invention and the prior art. See the *Graham* factors. As discussed above, Sung and van Loon fail to disclosure at least two limitations of Appellants' claims (i.e., an insulin sensitizer and specific proportions of small peptides). Note that free amino acids are not small peptides because the latter require at least two amino acids connected by peptide bonds. Therefore, in the absence of evidence to the contrary in the Action (such evidence being absent because the Examiner deemed it immaterial to perform the *Graham* analysis), it must be concluded as a matter of law from this failure to carry the Examiner's burden of going forward with acceptable evidence that a *prima facie* case of obviousness has not been established. The Examiner should have explicitly cited where each claim limitation is found in the prior art (and admitted when claim limitations are neither taught nor suggested by the prior art).

In summary, the failure of Sung to disclose the claimed invention is not remedied by the Examiner's attempt to modify that disclosure with van Loon. The Examiner did not comply with the requirements of *Graham* to establish a *prima facie* case of obviousness. In particular, he failed to show that the prior art rendered obvious a composition suitable for oral consumption comprising an insulin sensitizer and a peptide fraction of a protein hydrolysate, wherein at least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da and at least 20 molar% of peptides with a molecular weight below 2000 Da are present as di- and/or tripeptides. Appellants submit that there would be no motivation to combine the documents, no reason was provided for making the modifications to the prior art disclosures that are necessary to result in the claimed invention, and a reasonable expectation of success was lacking given the disparate objectives of the cited documents and the claimed invention. Finally, in contravention of *KSR* requirements, the Examiner also failed to determine whether the ability of Appellants' claimed composition to increase the insulin response in type 2 diabetic patients without lowering glucose levels (see pages 18-20 of Appellants' specification) is "more

than the predictable use of prior art elements according to their established functions" to rebut a *prima facie* case of obviousness.

As discussed above, the combination of Sung and van Loon documents does not render obvious the claimed invention because all limitations of independent claim 1 are not fairly taught or suggested by the cited documents. Moreover, claims depending from the independent claim are also not made obvious by the documents because the limitations of claim 1 are incorporated in the dependent claims. M.P.E.P. § 2143.03 citing *In re Fine*, 5 USPQ2d 1596 (Fed. Cir. 1988).

Appellants urge the Board to reverse this obviousness rejection because their invention as claimed would not have been obvious to a person of ordinary skill in the art at the time it was made.

35 U.S.C. 112 – Definiteness

B. Claims 1, 3, 5, 7-9, 11-12 and 19-21 were rejected under Section 112, second paragraph, as being allegedly "indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Appellants traverse.

It was alleged by the Examiner on page 7 of the Action that "it is not clear what the peptide fraction of a protein hydrolysate constituted." But the metes and bounds of the claims are clear to persons skilled in the art. A "protein hydrolysate" is a mixture of peptides and free amino acids produced by hydrolysis of protein(s) with a chemical or enzyme. See pages 8-10 of Appellants' specification. In general, the extent of hydrolysis determines the distribution of different lengths of peptide with the molar% of shorter peptides (e.g., di- and/or tripeptides) increasing as hydrolysis proceeds until free amino acids are liberated from the protein(s) as hydrolysis goes to completion (the size distribution of peptides can be determined by chromatography and mass spectrometry).

A "peptide fraction" is also known in the art as the part of the protein hydrolysate that comprises peptides and free amino acids. See the definition of "peptide fraction" on page 8 of the specification. Hydrolysis of protein results in a mixture of different peptides and free amino acids. Although the peptide fraction may include free amino acids, free amino acids are not peptides. Reciting the limitation that "at least 70 molar% of peptides

in the peptide fraction have a molecular weight below 2000 Da" is not a fishing expedition as characterized on page 7 of the Action. Instead, it a clear requirement imposed on the peptide fraction of independent claim 1 that at least 70 molar% of the peptides therein are small (i.e., peptides having a molecular weight below 2000 Da).

Appellants urge the Board to reverse this rejection because the pending claims are clear and definite.

Conclusion

For the reasons discussed above, the Examiner's rejections are improper and they should be reversed by the Board. Appellants submit that the pending claims are in condition for allowance, earnestly solicit an early Notice to that effect, and request that the nonelected claims be rejoined in this application.

Respectfully submitted,

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VIII. CLAIMS APPENDIX

1. A composition suitable for oral consumption comprising an insulin sensitizer and a peptide fraction of a protein hydrolysate, wherein at least 70 molar% of peptides in the peptide fraction have a molecular weight below 2000 Da and at least 20 molar% of peptides with a molecular weight below 2000 Da are present as di- and/or tripeptides.

3. A composition according to claim 1 further comprising at least one free amino acid selected from the group consisting of leucine, phenylalanine and arginine.

5. A composition according to claim 1, wherein the peptide fraction is comprised of peptides having molecular weights below 500 Da.

7. A composition according to claim 2, wherein most of the di- and/or tripeptides are comprised of proline at one end.

8. A composition according to claim 1, wherein at least 20% of proline present in the hydrolyzed protein is present in the di- and/or tripeptides.

9. A composition according to claim 1, wherein at least 30% of the tripeptides have a carboxy terminal proline.

11. A composition according to claim 1, wherein the insulin sensitizer is chromium, vanadium, niacin, corosilic acid, banana leaf extract, ginseng berry, Ginsensoside Re, cinnamon, methylhydroxy chalcone polymer, pterostilbene, biguanide or thiazolidinedione.

12. A dietetic product, or a pharmaceutical product, or a food or a food supplement comprising the composition according to claim 1.

19. A composition according to claim 1 further comprising at least one free amino acid selected from the group consisting of leucine, phenylalanine and arginine.

20. A composition according to claim 1 further comprising at least one free amino acid selected from the group consisting of leucine, phenylalanine and arginine.

21. A composition according to claim 8 further comprising at least one free amino acid selected from the group consisting of leucine, phenylalanine and arginine.

IX. EVIDENCE APPENDIX

None.

X. RELATED PROCEEDINGS APPENDIX

None.